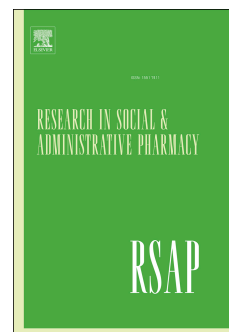


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**Patient access to medicines in two countries with similar health systems and differing medicines policies: Implications from a comprehensive literature review**

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The authors report no actual, potential or perceived conflict of interest with regard to this manuscript

## **Abstract**

## **Background**

Countries with similar health systems but different medicines policies might result in substantial medicines usage differences and resultant outcomes. The literature is sparse in this area.

## **Objective**

To review pharmaceutical policy research in New Zealand and Australia and discuss differences between the two countries and the impact these differences may have on subsequent medicine access.

## **Methods**

A review of the literature (2008 to 2016) was performed to identify relevant, peer-reviewed articles. Systematic searches were conducted across the six databases MEDLINE, PubMed, Science Direct, Springer Links, Scopus and Google Scholar. A further search of journals of high relevance was also conducted. Using content analysis, a narrative synthesis of pharmaceutical policy research influencing access to medicines in Australia and New Zealand was conducted. The results were critically assessed in the context of policy material available via grey literature from the respective countries.

## **Results**

Key elements regarding pharmaceutical policy were identified from the 35 research papers identified for this review. Through a content analysis, three broad categories of pharmaceutical policy were found, which potentially could influence patient access to medicines in each country; the national health system, pricing and reimbursement. Within these three categories, 9 subcategories were identified: national health policy, pharmacy system, marketing authorization and regulation, prescription to non-prescription medicine switch, orphan drug policies, generic medicine substitution, national pharmaceutical schedule and health technology assessment, patient co-payment and managed entry agreements.

## **Conclusions**

This review systematically evaluated the current literature and identified key areas of difference in policy between Australia and NZ. Australia appears to cover and reimburse a greater number of medicines, while New Zealand achieves much lower prices for medicines

than their Australian counterparts and has been more successful in controlling national pharmaceutical expenditure. Delays in patient access to new therapies in New Zealand have considerable implications for overall patient access to medicines; however, higher patient co-payments and relative pharmaceutical expenditure in Australia and its effect upon patient access to medicines must also be considered.

## Introduction

Pharmaceutical policy has been defined as the branch of health policy that “deals with the principles guiding decision making in the field of pharmaceuticals”,<sup>1</sup> with the aim of contributing towards the overall health and wellbeing in a given society within a healthcare system. Pharmaceutical policy is varied and includes licensing, pricing, formulary management, prescribing, pharmacy services, rational drug usage, pharmaceutical economics, access and affordability of medicines. The overall objectives of pharmaceutical policy involve maximising of access to medicines and ensuring the quality of medicinal products, whilst controlling the cost of health care and medicine and promoting rational drug use.<sup>2</sup>

Currently, medicines are the most common form of medical intervention and within Organisation for Economic Cooperation and Development (OECD) countries pharmaceutical expenditure ranges from 8-29% of healthcare spending.<sup>3-6</sup> However, medicines can be expensive and cost can act as a barrier to medicine access. Constraints in medicines access have important implications for patients **regarding** morbidity and mortality,<sup>3</sup> and thus this is an important topic of discussion amongst policy decision-makers in countries worldwide.

Healthcare costs have increased significantly over the past few decades and have been reported as “unsustainable” in advanced economies, without suitable reform. Both health and finance ministries need to work together to reach an optimal outcome for the budget and patient health.

Two countries that are renowned for minimising their cost increases are New Zealand and Australia, and thus it is important to compare and contrast their health policies and the subsequent effect on medicines access.

In New Zealand, the agency responsible for the decision on drug safety, registration and regulation in the country is the New Zealand Medicines and Medical Devices Safety Authority (Medsafe). A separate and independent authority that manages the pharmaceutical budget is the Pharmaceutical Management Agency (PHARMAC). PHARMAC oversee the reimbursement and purchasing of pharmaceuticals and medical devices for the community, as well as help the district health board’s (DHB’s) assess and procure the medicines and medical devices used in public hospitals.<sup>3,4</sup> Additionally, they maintain the country’s national pharmaceutical schedule and negotiate the national prices for new medicines.<sup>3</sup> This schedule represents the partly or fully subsidised medicines for New Zealand from the national

pharmaceutical budget and includes both medicines available from practitioners by prescription in hospitals or in the community.<sup>3</sup> PHARMAC use a capped budget, which has proven of international interest, but also has been a source of considerable debate, as this may impact on access to medicines, in particular new subsidised medicines.<sup>4</sup>

In Australia the registration of all medicines **is** evaluated by the Australian Therapeutic Goods Administration (TGA).<sup>5</sup> The Pharmaceutical Benefits Advisory Committee (PBAC), established under the National Health Act 1953, is an independent body appointed by the Australian government. PBAC assesses applications for each medicine **regarding** both clinical and cost-effectiveness for a particular indication (s) (see current revised PBAC guidelines 5.0).<sup>7</sup> Once a positive recommendation is made, the ultimate decision is made by the Minister of Health. Price negotiations may then be made by the Australian Department of Health.<sup>3,4,8</sup> Pharmaceuticals that are subsidised by the Australian Federal Government are then listed in the Pharmaceutical Benefits Scheme (PBS),<sup>3,4</sup> managed by the Australian Department of Health, under the Australian National Health Act 1953.<sup>4</sup> Expenditure under the PBS is not capped, to allow for new medicines to be added to the schedule, however, if a pharmaceutical will cost over \$20 million per year, the decision is referred to Cabinet for approval *within the set health budget*.

While both PHARMAC and PBAC consider cost-effectiveness, budget impact, utilise rebates and have risk-sharing agreements, PHARMAC is unique as it operates within a capped budget.<sup>3-5</sup> New medicines in NZ can only be added to the pharmaceutical schedule if the budget allows.<sup>4,5</sup> This is not the case in Australia where the Australian PBS does not operate within a defined funding envelope,<sup>4,5</sup> but under a *total health budget*.

Distinct differences exist between the two countries. These differences include the ability to negotiate independently, for example, PHARMAC is actively involved in bundling deals for several medicines as well as tendering contracts with single sponsors.<sup>4,5</sup> Policies at a patient level also exist, such as risk sharing and managed entry agreements with suppliers, the extent of co-payments and concessions for various population groups as well as medications available 'on' and 'off' prescription all have the capacity to influence patient access to medicines.<sup>5,6</sup>

The aim of this paper is to critically assess, review and document the status of pharmaceutical policy research in New Zealand and Australia and the impact of respective policies at the patient-level.

102 Specifically, the objectives were to: (i) compare medicines policy in Australia and New  
103 Zealand and how these differences impact on patient access to medicines and (ii) to make  
104 recommendations for future policy decision-makers to consider when considering medicines  
105 policy reform.

## Methods

### Defining Access

The definition of *access* to medicines can be varied amongst the literature. Access to medicine considers the listing of a medicine on the country's pharmaceutical schedule and also the ability of an individual, both financially and physically, to obtain and receive relevant care involving the respective medicine.<sup>3,10</sup> Access has also commonly been linked to medicine *availability* which is defined as whether a drug has obtained a relevant marketing authorization and registration under the relevant authority for drug safety, registration and regulation in the country.<sup>10,11</sup>

This study refers to outcomes that affect medicine access which encompass both the *availability* and *access* to medicines. Therefore, for the purposes of this study access to a medicine includes policies or factors that affect the *availability* of a medicine as well those that enable an individual (financially and physically) to obtain and receive relevant care involving the respective medicine.

### Search Strategy

The PRISMA guidelines for conducting systematic reviews were followed,<sup>9</sup> – Appendix 1.

This study used systematic searches between August 1st, 2015 and 1<sup>st</sup> July 2016 to identify peer-reviewed articles published between 2008 and July 2016. The search strategy was purposefully designed to be broad, in order to ensure all relevant material was included. The databases searched included: Medline, PubMed, Google Scholar, Springer Links, Science Direct and Scopus. The following relevant journals were also searched to ensure completeness for the same time period: PLoS One, PLoS Medicine, Nature, Health Policy, Pharmoeconomics, Medical Journal of Australia and the New Zealand Medical Journal. Our search included both mapped and un-mapped terms which are illustrated in Figure 1. Keywords included the following: (“Access” or “Availability” or “Accessibility”) and (“Pricing” or “Funding” or Reimbursement”) and (“Medicines” or “Drugs” or “Pharmaceuticals”) and (“Regulation” or “Policy”) and (“New Zealand” or “Australia”). The keywords were combined and integrated in database and journal searches. Within the conducted search “Boolean Operator” rules were utilised. The terms used were searched using ‘AND’ to combine the keywords listed and using ‘OR’ to remove search duplication



where possible. Reference lists of the retrieved articles were assessed for relevant articles that our searches may have missed. The process of identification, screening and inclusion of papers for this review is detailed in PRISMA format in Figure 1.

## Study Selection

Inclusion criteria were formulated that reflected the research aim. Firstly, papers were included if they referred to medicines policy and were investigating political and regulatory mechanisms in Australia and New Zealand by which medicines are accessed, funded and reimbursed and the mechanisms that define these aspects of pharmaceutical policy and medicine access. In addition, the studies must report outcomes in relation to patient access to medicines. Studies were excluded if not written in English or those in which the authors were unable to retrieve a full-text version of the study. It included original articles, reviews, commentaries and opinions if they described access, funding and reimbursement of medicines in New Zealand and Australia. It also excluded any studies that did not report policies or outcomes related to Australia or New Zealand. Inclusion and exclusion criteria are detailed in full in Table 1.

\*\* Insert Table 1 \*\*

## Data extraction

Study characteristics were extracted from all relevant studies and were recorded in an extraction table. One researcher (TG) compared and extracted data and discussed any discrepancies with other researchers (ZB, AS) when this was required. An overview of the identification process is documented in Figure 1.

## Analysis

Narrative synthesis of the articles was undertaken to compare policies and outcomes between the two countries. Themes and sub-themes were drawn from the data, until no more themes and sub-themes could be identified, and all important and differing policy areas with respect to access to medicines between Australian and New Zealand were considered. Through this analysis identification of how differing policies could have impact on patient access to pharmaceuticals were established.

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## Results

### Screening, selection and included studies

A diagrammatic depiction of the search strategy is included in Figure 1. The searches across all databases and journals identified 10,900 titles. The titles and abstracts of all retrieved articles were reviewed by TG for relevance. Studies were excluded if they did not meet the inclusion/exclusion criteria specified in the study. After removing duplicates and titles/abstracts unrelated to access to medicines in Australia or New Zealand, we identified (n=230) peer-reviewed articles for further review.

Sixty-three articles were relevant to access, funding and reimbursement of medicines in New Zealand and Australia and were considered against the inclusion/exclusion criteria of this review. A total of 30 articles were excluded at this stage. Two further studies were identified from the reference lists of the retrieved articles. The final number of articles therefore included for analysis in this review was 35 (Figure 1).

**\*\*Insert Figure 1\*\***

### Data collection and analysis

The data extracted from the 35 articles was documented; these articles generated three major themes with 9 major sub-themes; these are detailed in Table 2. The themes included: the national health system which was sub divided into five major sub-themes; national health policy, pharmacy system, marketing authorisation and regulation, prescription to non-prescription medicine switch and orphan drug policies. The second major theme was pricing; this included the sub-theme of generic medicine substitution. The final major theme was reimbursement; sub-themes included the national pharmaceutical schedule and health technology assessment, patient co-payments and managed entry agreements. Each theme and sub-theme is now described in more detail, with comparisons between Australian and New Zealand research.

These themes need to be considered within the context of the policies of each country and therefore an overview of these policies has been detailed in Table 3.

**\*\*Insert Table 2 and 3 \*\***

## 1. National Health System

The five sub-themes identified within the national health system theme include the national health policy, pharmacy system, marketing authorization and regulation, prescription to non-prescription medicine switch and orphan drug policies.

### *i. National Health Policy*

Both Australia and New Zealand have a publically funded health system, alongside a private hospital sector.<sup>12,13</sup> In Australia, the national government funds two thirds of total healthcare spending while the other third is funded by other, lower levels of the national and state government.<sup>4,5,12</sup> In New Zealand 80% of expenditure on health care is publically funded, and 20 District Health Boards across New Zealand are responsible for the public health services in their respective populations.<sup>4,5,13</sup> The regulation and funding of medicines in Australia is determined by the National Medicines policy. This policy has the overall aim to ‘meet medication and related service needs so that optimal health outcomes and economic objectives are achieved’.<sup>12</sup> This policy has four key objectives to; ensure medicines meet a standard of safety, quality and efficacy, ensure timely access to necessary medicines at an affordable cost to the individual and the Australian community and ensure the quality use of medicines and the maintenance and regulation of the Australian medicines industry.<sup>12</sup> In New Zealand ‘Medicines New Zealand’ provides a framework document to determine the direction for agencies and stakeholders in the New Zealand medicines sector. It aims to; ‘deliver equitable access to safe quality medicines used in the most effective ways possible’, promote a transparent, accessible and trusted medicine sector and to deliver affordable medicines that meet the needs of New Zealander’s and is sustainable.<sup>4,5,13</sup> Medicines policy in New Zealand includes the pharmaceutical subsidy card (allowing prescriptions to be filled at reduced or no cost), high use health cards, community services cards (for lower income families), disability allowances and coverage by the accident compensation cooperation (ACC) in the case of an accident which requires use of medicines.<sup>4,5,13</sup>

Patients have access to medicines in both countries through community pharmacies and hospitals, as thus we must consider both critical elements when evaluating access to medicines for patients.<sup>4,5,12,13</sup>

### *ii The Pharmacy System*

The pharmacy system in both Australia and New Zealand primarily provide dispensing services for prescription-only medicines, as well as providing a range of over-the-counter medicines and patient-related services including, the provision of **health-related** information, medications management, preventative care and/or clinical interventions.<sup>4,5,12,13</sup>

There are over 6,663 pharmacies and chemists throughout Australia,<sup>14</sup> with pharmacy ownership restricted to registered pharmacists. Additional programmes to improve access and use of medicines have been established; medication adherence, medication management, rural support as well as Aboriginal and Torres Strait Islander programs have been developed and implemented in Australia with the aim to improve access to medicines as well as support quality community pharmacy services. The programs often include allowances to approved pharmacies delivering and distributing medicines subsidised on the PBS.<sup>15</sup> In December 2015 the DOH stated that under the Sixth Community Pharmacy Agreement there would be up to \$1.6 billion in funding available, consisting of \$613 million for the continuation of programs and services from the fifth CPA, \$50 million for a new pharmacy trial program and up to \$600 million for new and expanded programs.<sup>16</sup>

In New Zealand, there are close to 1000 community pharmacies,<sup>17</sup> distributed across the country. The pharmacies tend to operate under contractual relationships with district health boards and receive funding for providing particular services to patients, most notably the long-term conditions (LTC) service and services for primary healthcare. The LTC service provides support to patients who have at least one long-term health condition, who have been identified as having issues with medication adherence. The aim is for these patients to become self-managing with their medications.<sup>18</sup> The pharmacy self-care programme which is a health education programme delivered through pharmacies.<sup>13</sup> The latter programme aims to improve access to medicines and promote the quality of medicines **using** pharmacies as primary health care centres.<sup>6,13</sup> It consists of online training modules for pharmacists and pharmacy staff and uses 'fact cards' as resources for patients. Together these provide relevant and critical information and support patient consultations.<sup>6,13</sup>

### ***iii. Marketing Authorization and Regulation***

Marketing authorisation and regulation involves the assessment of a medicine, by the relevant regulatory authority, before the medicine is authorised for marketing and subsidy evaluation. This is a critical step in enhancing the availability (and access) of medicines.<sup>4,5,10,12,13,15,19,20</sup> This process generally includes substantial scientific evaluation of the benefits and risks of

medicines to determine whether the drug is safe for use and for a specific indication(s)<sup>5,20</sup>. In Australia, the Therapeutic Goods Administration (TGA) evaluates applications for the registration of new medicines and indications and ensures the acceptable quality, safety and efficacy of new medicines and/or indications.<sup>3,4,12</sup> Where medicines meet these standards, they are included on the Australian Register of Therapeutic Goods.<sup>12</sup> In Australia, parallel processing of medicines is possible; in contrast this is not the case in New Zealand.<sup>3,4,5,12,30</sup> Parallel processing allows submission to the TGA for medicine registration to be conducted at the same time as submission to the Pharmaceutical Benefits Advisory Committee (PBAC), who provide a clinical and economic evaluation, and subsequent recommendation to the Minister of Health regarding whether it should be listed in the Pharmaceutical Benefits Scheme (PBS).<sup>3,4,30</sup> The risk associated with parallel processing in Australia is offset by cost-recovery fees paid by the sponsor company to cover ‘resources specific to the subsidised access evaluation’ and ‘agreement that the outcome of the assessment by the subsidised access agency will not be made publically available until the regulatory agency has made a decision’.<sup>5</sup> In New Zealand, Medsafe is responsible for applications for registration and marketing of new medicines in the country.<sup>3,4,5,13</sup> Medsafe, in a similar manner to the Australian TGA, considers the efficacy, safety and quality of medicines both through pre-marketing evaluation and post-marketing monitoring.<sup>3,4,5,13</sup>

Both countries estimate to have a registration period of 52 weeks, however, Australia had a shorter duration from regulatory submission to subsidised access of 72 weeks compared with 84 weeks in New Zealand.<sup>5</sup> This difference was most likely reflective of parallel processing in Australia.<sup>5</sup> Parallel (regulatory) processing has been acknowledged to potentially enable ‘time efficiencies to be gained’.<sup>5</sup> Ragupathy et al.,<sup>30</sup> considered the age of entities licensed (registered) across four countries (United States of America, United Kingdom, Australia and New Zealand). In comparison, Australia and New Zealand’s entity age differed, with entities licensed in New Zealand on average being older than those licensed in Australia. The median age of licensing was 7795 days in Australia and 8936 days in NZ.<sup>30</sup> Similarly, Cook et al.,<sup>5</sup> found critical differences in the time taken from regulatory submission to subsidised access to medicines. Another study by Wonder et al.<sup>1</sup> compared the timeliness of availability and access to medicines between Australia and New Zealand. Of 59 medicines listed in Australia and New Zealand between 2000 and 2009, registration occurred on average sooner in Australia than in NZ with a mean difference of 9 months. In particular, 43 of the 59 medicines were registered in Australia before NZ.<sup>1</sup> The timely availability of (new) medicines through

registration and thus approval for marketing has been noted as a critical indication in enabling downstream access to medicines by many studies.<sup>3,4,5,10,12,13,15,20-29,30</sup>

#### *iv. Prescription to Non-Prescription Medicine Switch*

Prescription to non-prescription switch or 'switch', also known as reclassification or down scheduling, is the movement of medicines 'down' medicine schedules to facilitate more convenient and timely access to medicines for patients.<sup>6,19</sup> Switch has been utilised to enable self-care, patient-centred care programmes and improving patient access to medicines.<sup>6,19</sup> Australia and New Zealand both have three medicine schedules; *pharmacist-* only, *pharmacy*-only and general sales.<sup>19</sup> Australia does not have an overall governmental position on medicine switch and The Secretary to the Department of Health, or their respective delegates make the final decision on switch.<sup>6</sup> In New Zealand the Medicines Classification Committee (MCC) recommends classifications of medicines.<sup>6</sup> Gauld et al.,<sup>6</sup> investigated factors that both enabled and prevented switch in Australia compared to New Zealand. The study found that New Zealand was more active in switching medicines from prescription to non-prescription, with New Zealand approving 13 of 25 medicines for switch between 2000 and 2011, in comparison Australia approving 9 of 22 medicines in the same time period.<sup>6</sup> Enabling factors for switch to occur were described; in New Zealand enablers included a small country, pharmacist only schedule, openness to different ideas, industry confidence in the MCC, confidence in Medsafe, confidence in pharmacy and consumers, ability to advertise over-the-counter medicines and a potential to influence switch in Australia.<sup>6</sup> Australia identified less enabling factors including, pharmacist only schedule, confidence in pharmacy and consumers.<sup>6</sup> Barriers to switch were also reported, more were described by Australia; advertising restrictions, risk adverse committee, immediate generic entry and an inability to see the regulator were all listed. In New Zealand the major barrier to switch was the recognition of a low co-payment on prescriptions and immediate generic entry.<sup>6</sup> A separate study considered factors affecting 'switch';<sup>19</sup> barriers to 'switch' often appeared to dominate over enablers. In Australia barriers included 'committee constitution, individuals, events, politics, advertising limitations and rigidity'.<sup>19</sup> In New Zealand market exclusivity and transparency, population size and the low co-payment on prescription medicines were key barriers. Both studies recognised that while 'switch' had the capacity to enhance patient access to medicines in a convenient location, considerations of the safety of these medicines off-prescription, introduction of generic medicines, low co-payments on prescription



medicines in New Zealand and a limited market size were considered by relevant committees in Australia and New Zealand.<sup>6,19</sup>

#### iv. *Orphan Drug Policies*

Orphan drugs are medicines or vaccines intended to treat, prevent or diagnose a rare disease.<sup>10</sup> Examples of rare diseases include genetic diseases, rare cancers, infectious tropical diseases and degenerative diseases.<sup>10</sup> The definition of rare diseases varies across jurisdictions but typically considers disease prevalence, severity and existence of alternative therapeutic options.<sup>10</sup> In Australia, the definition of an Orphan Drug is a condition with a prevalence of not more than 5 in 10,000 people which is life-threatening or seriously debilitating condition and no existing therapeutic goods for prevention, diagnosis or treatment or significant benefit.<sup>10</sup>

The nature of rare diseases means that there are limited numbers of patients who have these conditions; drug development therefore is also limited and/or access to these medicines can be difficult, due to high cost and unfavourable cost effectiveness ratios in economic analyses.<sup>10,11</sup> Policies and legislation regarding orphan drugs intends to address the challenges of exorbitant costs of product development and narrow profit potential due to the smaller market size for each indication. Orphan drug policies aim to enhance both availability and access of these medicines and includes a variety of incentives to encourage research, development and marketing as well as pre-licensing access and compassionate use programmes into treatments for rare diseases.<sup>10,11</sup>

Both Australia and New Zealand recognise rare diseases and orphan drugs. Australia introduced an orphan drugs act under the amended Therapeutic Goods Act in 1997.<sup>10</sup> This act includes independent orphan drug designation and marketing authorization/regulatory approval **with fee reductions** for orphan drugs.<sup>10,11</sup> Under the orphan drugs program there is a 100% fee waiver.<sup>31</sup> In terms of enhancing availability of these drugs, Australia also has in place pre-licensing access and regulatory assistance for manufacturers.<sup>10</sup> Australia implemented orphan drug policies which look to enhance their access to patients. In particular, orphan drugs may be considered for subsidisation under Australia's Life Saving Drugs Programme (LSDP) for eligible patients, which provides subsidised access to drugs for rare conditions.<sup>10,11</sup>



In contrast, New Zealand does not include mention of orphan drugs in legislation. However, in 2014 PHARMAC aimed to improve access to medications for rare disorders and requested feedback.<sup>32</sup> Currently there are ten medicines approved for funding via this pilot scheme; PHARMAC has reported that it intends to continue to make these medications available.<sup>32</sup>

## 2. Pricing

There are direct and indirect impacts of pricing on patient access to medicines. Firstly, regarding subsidised medicines, the price paid will dictate which medicines may be funded by the government or relevant regulatory agency, and in some cases (i.e. in New Zealand) this may impact on how many medicines (due to the capped nature of the budget).<sup>3,4,12,13,20</sup> Price also has a direct impact on patient access to medicines in the case of non-subsidised (high cost) medicines,<sup>3,4,12,13,20</sup> as these become out-of-pocket costs for patients.

Both Australia and New Zealand utilise varying degrees of reference and value based pricing. In Australia, pharmaceutical companies apply for PBS listing following positive approval for marketing by the TGA (or with parallel processing, simultaneously) and these applications are evaluated by PBAC.<sup>3,4,12,13,20,21</sup> Price negotiations may then be made by the Australian Department of Health.<sup>3,4,8</sup> Listing of new medicines are generally based upon reference pricing (cost minimisation), where medicine efficacy and safety are considered relative to existing listed medicines. An alternative used is value based pricing, where medicines are recommended for funding if they meet an acceptable incremental cost-effectiveness ratio (ICER).<sup>3,4,12,13,20,21,33</sup>

In New Zealand, PHARMAC utilise several pricing techniques to fund medicines within their fixed medicines budget.<sup>3,4,12,13,20,21,33</sup> These include price negotiations, sole or generic supply contract tendering, reference pricing for medicines with similar therapeutic effects and price rebates.<sup>3,4,12,13,20,21,33</sup> PHARMAC also utilise rebates, expenditure caps (when sales exceed a set limit the manufacturer will cover some or all of the costs to supply the medicine above this cap) and cross product agreements (an agreement to subsidise a medicine dependent on a price reduction on one or a number of medicines already subsidised on the national schedule) in order to lower the price paid.<sup>33-36</sup>

A stark difference between the Australian and New Zealand pricing and reimbursement strategies is that PHARMAC's operates within a capped budget, which is not the case in Australia. In Australia the total Health Expenditure is capped, however within that the

proportion is spent by the PBS is not capped, this is to allow for new medicines to be added.<sup>3,4,5,23</sup> Morgan et al.,<sup>20</sup> investigated basic pharmaceutical policy structures and performance indicators for the seven difference countries, including Australia and New Zealand, and discovered that the growth rate for pharmaceutical expenditure in relation to health care expenditure and national income from 1995 to 2005 was the lowest in New Zealand (2.5% per annum) compared to all countries in the study while Australia had a growth rate of 6.3% per annum.<sup>20</sup> It is acknowledged that this slow rate of growth may reflect the use of a capped budget in the operation of the New Zealand national pharmaceutical schedule.<sup>20</sup> A 2011 study by Spinks et al.,<sup>33</sup> compares medicine prices for many select drugs from Australia and New Zealand. New Zealand attained lower prices for 29 of the 34 drugs included in the study with a saving of AU \$0.93 billion if purchased at the New Zealand price.<sup>33</sup> It is noted that a more effective use of competition and a competitive tender process in the purchasing of medicines by New Zealand and its PHARMAC may be the critical factor in the differences in prices paid for medicines.<sup>33</sup> Interestingly, an analysis of medicine prices in New Zealand compared to 16 European countries found that New Zealand prices were found in the lowest quartile for five medicines and in the highest quartile for seven other products for a basket of 14 medicines.<sup>34</sup> Analysis of these results highlighted that the lower priced were medicines that had a generic alternative available. All medicines in the study were reimbursed in New Zealand so this difference was recognised to likely be due to New Zealand's success in possessing lower prices for generic products as well as uncertainty on the 'real price' paid due to PHARMAC's desire to release the listed price alone and not the true price paid (and discount negotiated) for the agency to contain pharmaceutical expenditure.<sup>34</sup>

### ***Generic Medicine Substitution***

Generic medicines are defined by the World Health Organisation (WHO) as "a pharmaceutical product, usually intended to be interchangeable with an innovator product that is manufactured without a licence from the innovator company and marketed after the expiry date of the patent or other exclusive rights".<sup>35</sup> Generic medicines are identical to the original innovator product in terms of safety, quality, efficacy, dosage and dosage form, product strength and the administration route. Generic medicines are also utilised for the same use or indication as the original innovator product.<sup>24,26,35</sup> Several studies note that generic medicines nearly always emerge with lower prices than originator products and thus have the capacity to reduce pharmaceutical expenditure, produce significant price savings,

allow subsidisation of additional medicines thus enhancing access to new medicines for patients.<sup>13,24,26,35</sup> Hassali et al.<sup>35</sup> explored what role generic medicines played in the health system of eight selected countries including Australia. The study reported that generic medicines were between 20% and 90% less expensive compared to the original innovator medicines.<sup>35</sup> Furthermore, the study recognised that Australia, utilising referencing pricing, opened the PBS to generic medicines. Australia, in 2005 also implemented a 12.5% price reduction policy which indicated that the first new generic pharmaceutical for listing on the PBS must be priced at least 12.5% below the current lowest priced brand.<sup>35</sup> In 2011 this was increased to 16% (36). Additionally, since 2008 pharmacists were paid to dispense cheaper brands, this was updated in the 6CPA and is known as the Premium Free Dispensing Incentive.<sup>36</sup> In particular, when they dispense a substitutable, premium-free PBS medicine they receive a premium free dispensing incentive and equal to AUD \$1.78.<sup>35,36</sup>

Changes to the pricing system including these mandatory price reductions and disclosure all are estimated over the 2008/09 to 2017/18 period to save the Australian health system AU\$ 6.4 billion.<sup>35</sup>

A study that reported the rate of Australian community pharmacist's generic substitution and cost-savings achieved for patients, in addition to patient acceptance of generic medicines was conducted.<sup>24</sup> Generics were recommended by pharmacists in 96% of the prescription items eligible for substitution in the study. It was also revealed that due to the substitution, patient medicines expenditure decreased by approximately 21%. The high rate of substitution was thought to link to Australia's generic medicine substitution policy and the dispensing incentives implemented by the country.<sup>24</sup> However, the patient declined the opportunity to switch to a generic medicine as offered in 21.5% of cases. This may reflect a patient perception of these medicines are inferior quality or brand loyalty.<sup>24</sup>

New Zealand has several policies to support the listing and uptake of generic medicines. In particular, these policies centred on reference pricing, competitive tendering and creation of competition between manufacturers of generic medicines.<sup>13</sup> In a study by Spinks and colleagues,<sup>33</sup> the differences in prices paid for a select group of medicines found that New Zealand paid lower prices for generic products than Australia. It must be noted that the comparison was limited to the ten generic medicines in the study and there is not full transparency with the actual price in NZ. However, if this is taken at face-value, it is

speculated that Australia could achieve savings of AU ~\$460 million by purchasing generics at the New Zealand price.<sup>33</sup>

Many studies in this review recognise the differences in pricing of generic medicines to be the likely result of differences in governmental and institutional pricing policies between Australia and New Zealand.<sup>3,4,12,13,24,26,33,35</sup>

## Reimbursement

The coverage and reimbursement of medicines has most often been considered by the literature as the single most important factor determining patient access to medicines in high income countries such as Australia and New Zealand.<sup>3,4,5,10-13,19,20,28-30,33-35,37-43</sup> In particular, many medicines that are not subsidised by a third party are often unaffordable for individual patients and so access to these medicines will be extremely limited.<sup>3,4,5,10-13,19,20,28-30,33-35,37-43</sup> Furthermore, even in the case that medicines are reimbursed by the national government,<sup>12,13</sup> patient cost sharing schemes (in terms of patient co-payments or co-insurance) can still lead to inadequacies in medicines access for patients.<sup>3,4,5,10-13,19,20,28-30,33-35,37-43</sup> The theme of reimbursement covers three major sub-themes including national Pharmaceutical Schedule & Health Technology Assessment, Patient Co-Payments and Managed Entry Agreements.

### *National Pharmaceutical Schedule and Health Technology Assessment*

Both countries utilise ‘subsidised access processes’ whereby the assessment of value of a medicine (also known as its cost-effectiveness) is determined by the country’s health technology assessment body.<sup>3,4,5</sup> In Australia, the subsidisation of medicines is achieved via a positive recommendation by PBAC and subsequent approval by the Minister of Health, the new medicine and indication(s) is then listed on the PBS.<sup>4,5,12,15,27</sup> PBAC does not operate under a capped budget however an overall capped health budget; any medicine expected to exceed AU \$20 million per year must be approved by Cabinet.<sup>4,5,12,15,27</sup> In New Zealand, PHARMAC operates the national pharmaceutical schedule for subsidised medicines and lists new medicines, indications and medical devices on the national schedule for New Zealand. PHARMAC administers the schedule alone and the New Zealand government or judiciary cannot block any listing.<sup>4,5,13,20,28</sup> PHARMAC operates within a defined funding envelope which allows a fixed budget for listing of new medicines each year.<sup>4,5,13,20,28</sup>

Both PBAC in Australia and PHARMAC in New Zealand utilise health technology assessment and economic evaluation in their decision making for the addition of (new) medicines to the national pharmaceutical schedule. PBAC consider efficacy, safety, cost-effectiveness and budget impact and utilises several methods of economic analysis including cost utility/ effectiveness analysis and cost minimisation analysis (CUA/CEA and CMA).<sup>4,5,12,15,27</sup> Between 2015 and 2016 the PBAC criteria was revised; the revised document is now available (version 5.0) and reflect the changes that have occurred regarding health technology assessment, however the key factors for decision making are essentially the same as they have been in past guidelines.<sup>7</sup>

PHARMAC has recently moved toward implementing a new set of criteria named the 'Factors for Consideration' which includes need, health benefit, costs and savings and suitability and is available to view on their website.<sup>4,5,13,20,28,44</sup> The Factors for Consideration are represented in a circular diagram. Within the four dimensions listed above there are also three levels; the impact to the person, the person's family, whanau and wider society and also to the broader health system. The extent to which any one particular factor is relevant, if at all, and the influence of each factor is for PHARMAC to determine on each occasion within the context of its legal obligations.<sup>4,5,13,20,28,44</sup> PHARMAC primarily utilise cost-utility analysis (CUA) in economic analyses.<sup>4,5,13,20,28</sup>

Several studies in this review directly compared access to medicines between Australia and New Zealand, where access to medicines was defined as a positive listing on the national pharmaceutical schedule. Many studies have noted that the number of medicines subsidised in New Zealand was less than the number subsidised in Australia.<sup>3,4,5,30,33,41</sup> The comparison of pharmaceutical prices by Wonder and Milne,<sup>3</sup> revealed that, of 139 new medicines listed on the PBS in Australia, only 59 of these were listed on the New Zealand PHARMAC schedule. The study also recognised that marketing authorization and registration occurred sooner in Australia; 53 of the 59 medicines reimbursed in New Zealand were reimbursed in Australia first with a mean difference of 32.7 months.<sup>3</sup> The study considers that the differences in access between countries may have been due to differences in the financial constraints of each agency,<sup>1</sup> in addition to the Australia implementing a greater number of risk sharing agreements to manage financial risk and limit excess costs.<sup>3</sup>

Moodie et al.<sup>23</sup> provide an interesting insight into differences in access. Their paper discusses the effect of PHARMAC's capped budget and notes that this cap results in extra time in

funding decisions needed to ensure value for money and an ability to forecast expenditure. Moreover, the paper discusses New Zealand's hesitance to fund 'me-too' medicines without the presence of an obvious financial or clinical benefit.<sup>23</sup>

Another study compared access to a select number of licensed and subsidized medicines including Australia and New Zealand.<sup>30</sup> It was discovered that New Zealand subsidised the oldest and smallest number of medicines included in the analysis while Australia subsidised a greater number of medicines and these tended to be newer (567 entities and 30 innovative entities subsidised in the Australian PBS compared to 503 entities and 19 innovative entities subsidised by PHARMAC in New Zealand).<sup>30</sup> However, in Australia, inequities in access to higher cost medicines were experienced between public and private hospitals. This occurred due to funding mismatch where a cap on the funding available for public hospitals and the lack of a cap on the PBS often led to a lack of funds for higher cost medicines in public hospitals compared to higher income private hospitals leading to differential access to these medicines between hospitals.<sup>42</sup>

### ***Patient Co-Payments***

Patient access to medicines is likely to be constrained by patient co-payments or coinsurance, particularly when these costs are considerable.<sup>10,11,12,13</sup> Patient co-payments can have a negative impact upon the affordability and thus access to medicines, particularly affecting lower income patients.<sup>25</sup> Medicine co-payments by patients in Australia are implemented under two categories for medicines on the PBS. The first, for 'general' patients are maximum co-payments of AU \$38.30 while concession card holders (seniors, lower income holders and some 'other' groups) pay AU \$6.20.<sup>5,11</sup> New Zealand patients pay NZ\$ 5 for prescription medicines subsidised by PHARMAC for all patients besides children less than 13 years which receive subsidised medicines free of charge.<sup>5</sup> Both countries have in place 'catastrophic coverage' which are policies that protect against the risk of excessive out of pocket expenditure by patients.<sup>10,11</sup> In Australia safety net thresholds of AU \$1457.70 for general patients and AU \$372 for concessional patients are present while in New Zealand a maximum of 20 co-payments per family per year is required (NZ \$100) before no co-payment is required to access these medicines.<sup>3,4,12,13,23,25</sup> Morgan et al.,<sup>20</sup> a study that reviewed pharmaceutical policy structures and performance indicators for seven countries including Australia and New Zealand, that the co-payments encountered by 'general' patients



in Australia were high compared to other countries with national drug benefit programmes, particularly compared to New Zealand.

One study recognised that following an increase in patient co-payments in Australia for 17 selected medicine on the PBS, significant decreases in the volume of dispensed medicines for 12 of the 17 categories occurred. This result suggests that increases in patient co-payments for medicines can significantly impact the ability of patients to afford and thus access these medicines.<sup>45</sup>

Both Australia and New Zealand possess little government regulation for medicines not listed on the national schedule, thus manufacturers are able to set prices at market entry. This was often the case for high-cost medicines and orphan drugs leading to substantial patient co-payments.<sup>10,11,12,13,42</sup>

### ***Managed Entry Agreements***

Managed entry agreements (MEA's), also known as patient access or risk sharing schemes are utilised in both Australia and New Zealand; these are utilised as unconventional access agreements for medicines. These exist between third party (healthcare) payers and pharmaceutical companies for conditional coverage of specific medicines.<sup>46,48</sup> These schemes allow coverage or reimbursement of medicines subject to specific conditions and address uncertainty regarding the likely efficacy of these medicines.<sup>46-48</sup>

These managed entry agreements exist in three formats; outcome based, evidence generation and financial agreements. The first (outcome based) links the reimbursement of the medicine to clinical outcomes, measured with regard to patient quality or quantity of life. Evidence generation is utilised where a positive reimbursement decision is dependent upon the collection of additional evidence for the respective pharmaceutical.<sup>46</sup> In the case of both of these access schemes, the prices of these medicines will be reduced if outcome targets are not met or the generation of additional evidence is not provided.<sup>10</sup> The third type of MEA is the financially based schemes, which require company contributions to the cost of the particular pharmaceutical product i.e. through discounts, rebates, cost-capping, price-volume agreements or utilisation caps.<sup>10,46</sup> A 2015 study,<sup>46</sup> reviewed the number of patient access schemes in Australia and New Zealand amongst other countries, and found that 98 schemes were present in Australia and only 5 in New Zealand. All five managed entry agreements in New Zealand were financially based, whilst 41 of 74 schemes in Australia were hybrid

schemes that included both a financial and an outcome component. Three schemes in Australia were based upon evidence generation.<sup>46</sup> A separate study,<sup>47</sup> investigated the number of managed entry agreements in Australia and identified 71 MEA's in use with 26 restricted to use in hospitals. Managed entry agreements were most often utilised to allow access to (higher cost or innovative) medicines for patients, that may not otherwise be funded based on health technology assessment (due to uncertainty regarding cost-effectiveness or budget impact).<sup>10,46-48</sup>



## Discussion

This review provides a systematic and comprehensive literature review between 2008 and 2016 of pharmaceutical policies in Australia and New Zealand and how these policies may influence access to medicines in each country. It is vital to review this research in the context of the current policies of respective countries and therefore we have also provided a summary of pharmaceutical policies and practices in Australia and New Zealand and how the implementation of these policies may have influenced medicines access in each country.

This review provides a novel consolidation of medicines access research, based on differences in policy, and therefore adds to the current literature on the topic. To date, to our knowledge, no other review has encompassed the effect on medicines access outcomes in this manner. The overarching goal was to provide a comprehensive review, to be used by policy decision-makers to better inform future policy reform. The review acknowledged 3 major levels of pharmaceutical policy with 9 subcategories. Differences in marketing authorization, medicine switch, orphan drug and pricing and reimbursement policies between the two countries were acknowledged to result in differential access to medicines.

Australia and New Zealand have similar national health systems; Australia and New Zealand are primarily publicly funded health systems and each utilise a major national medicines policy. This medicines policy endeavours to provide access to medicines for patients ensuring medicine safety, quality and effectiveness at a reasonable cost. Cost is deemed one of the most important barriers to access of medicines by both countries.<sup>4,5,6,12,13,20</sup> Pharmacies are recognised in both countries as a means to provide and improve access to medicines.<sup>4,5,6,12,13</sup>

However, there are notable differences between the two countries. Marketing authorisation policies differ between the two countries. Whilst both countries have implemented a single national regulatory authority (TGA in Australia, Medsafe in New Zealand) and both consider the efficacy, safety and quality of medicines, Australia had implemented a parallel processing policy while New Zealand had not. This policy has enabled for the submission of medicine registration to be conducted at the same time as submission for medicine subsidisation on the national reimbursement list. This difference has led to significantly shorter time frames between regulatory submission to subsidised access in Australia compared to New Zealand.<sup>3,4,5,10,12,13,15,20,29,30</sup> As mentioned earlier both countries were estimated to have a registration period of 52 weeks, Australia had a minimum time from regulatory submission to

subsidised access of 72 weeks as opposed to 84 weeks in New Zealand. Additionally, a study of seven countries within the Asia Pacific region (Australia, New Zealand, China, Japan, Korea, Taiwan and Thailand) by Cook et al.,<sup>5</sup> critical differences were seen in time taken from regulatory submission to subsidised access to medicines. Moving forward, having a separate and parallel system that evaluates medicine registration and subsidisation may be one way of shortening this time and thus improve access.

Reclassification of medicines from prescription to non-prescription was found to be more common in New Zealand due to a variety of factors, most notably the national confidence in pharmacists, consumers and Medsafe. Political rigidity in Australia has been reported to limit medicine 'switch'.<sup>6,19</sup> 'Switch' utilised in a responsible and safe manner was recognised to promote patient-centred care and thus had the capacity to improve patient access to medicines.<sup>6,19</sup> Reclassification in community pharmacy has been reported to impact accessibility of medicines in nine European countries, as post-deregulation there was an associated increase in pharmacy establishment.<sup>34</sup> However, this study also noted that this tended to be in urban areas. Therefore, whilst reclassification may increase access, policy makers in Australia and NZ should also bear in mind equitable access – as described by Vogler and colleagues.<sup>34</sup>

Orphan drug legislation was implemented in Australia, in contrast New Zealand does not have such as legislation, except for a NZ \$5 million fund for high cost medicines for rare disorders.<sup>10,11</sup> The use of this legislation in Australia promoted the availability of, and access to, orphan drugs in the country. No study quantitatively compared access to orphan drugs between Australia and New Zealand, however, due to variances in pharmaceutical policy relevant to these medicines differences in access may exist. Future research is warranted in this area. Managed entry agreements were innovative access schemes to encourage and allow access to medicines that lacked sufficient evidence for reimbursement or to allow access to high cost medicines including orphan drugs. Australia implemented a much larger number of managed entry agreements compared to other countries (including New Zealand).<sup>46-48</sup>

Higher prices of medicines often limit patient access twofold; higher prices reduce the likelihood of a listing on the national reimbursement schedule, as well as increased out-of-pocket costs for patients for non-subsidised, often higher cost, medicines. Both countries utilised different pricing policies -- reference and value based pricing. Medicine prices in New Zealand were acknowledged to be consistently lower than those prices in Australia,

especially with regard to generic medicines.<sup>13,20,21,33,34</sup> Effective use of competition, a competitive tendering process and particularly, the use of a fixed, capped budget by PHARMAC in New Zealand were considered important factors in the success of PHARMAC in negotiating these lower prices, when compared to the prices of medicines in Australia.<sup>3,4,5,13,20,21,24,26,33-35</sup> Currently, in Australia the DOH is responsible for negotiating prices of pharmaceuticals with the manufacturer; competition between pharmaceutical manufacturers and competitive tendering are unlikely to be successful for generic medications as multiple generics of the same medicine are available on the PBS.

Both countries use similar criteria for the selection of medicines for reimbursement, i.e. health technology assessment is used by PBAC and PHARMAC.<sup>3,4,5,30,33,41</sup> Listing on the reimbursement schedule of medicines is undoubtedly the most important factor determining patient access to medicines. However, although the use of a fixed, capped, budget in New Zealand by PHARMAC has ultimately kept pharmaceutical spending down, it has been linked to the considerably lower number of medicines reimbursed in New Zealand compared to Australia. This has led to many patients having to pay out-of-pocket for treatment, if available privately. NZ medicines policy has enlisted a number of avenues to access medicines that are not available on the listed schedule. On the other hand, higher co-payments for patients can also pose a significant barrier to medicine access, regardless of the availability of medicines. This review recognised that Australia had much higher patient co-payments for medicines at almost 8 times the payments required for patients in New Zealand. Australia does however have in place lower co-payments for concession card holders, which include elderly, lower income, eligible veterans. In both countries, those patients that exceed a specified threshold of spending on schedule-listed medicines are in place to prevent excessive out of pocket costs for patients. The limit for 'general' Australian patients was approximately 13 times the limit compared to New Zealand patients, and for concession card holders in Australia was around 3 times higher than that for New Zealand patients.<sup>4,5,10,11,12,13,23,25,30,37</sup> When compared to overseas, New Zealand has one of the "most generous prescription charge regimes in the world" (beehive); the United Kingdom prescription charges are equivalent of approximately 1/3 of that of Australia, Canada's costs vary by province but often is based on household income. Pressure on pharmacies with the reduced income led to many pharmacies charging additional fees, for example after-hours fees, which then were passed on to the patient. This is one avenue that can be considered outside of New Zealand to reduce overall spending. Taken together, both countries exhibit

different policies that may act as barriers to access of medicines. Whilst NZ has much more restricted breadth of medicines that are listed on the schedule, Australian patients out-of-pocket costs are generally much higher, which could impact also on access.

Our definition of access to medicines included the availability in addition to financial and physical ability to obtain and receive relevant care involving the respective medicine(s). Australia and New Zealand both illustrate complex, highly efficient and functioning pharmaceutical systems which appear to both promote in some cases, but restrict access to medicines in others. Australia appears to have in place several policies, most notably parallel processing which enhances medicine *availability* in a manner that is not replicated in many other health systems around the globe. As mentioned, this could be something that policy decision-makers (including those in New Zealand) consider to reduce the time between registration to review for reimbursement.

At a higher level, the themes and sub-themes that were identified in this review have the potential to influence future frameworks for policy analysis. In 2013, Bigdeli and colleagues,<sup>50</sup> reviewed access to medicines from a health system perspective; they acknowledged that the access to medicines barriers are: “complex and interconnected”. In addition, they believe that the existing frameworks only partly take into account the full range of barriers. The authors of the review suggested a shift from the existing frameworks available to take into consideration these complex interactions and barriers. We believe that our review adds to this model or a future reformed model; we must consider the patient outcomes at the centre of the policy framework – as Bigdeli has – and also ensure that we consider avenues for access of new and emerging medicines, including those that lack enough evidence to be fully subsidised through a national listed-schedule.<sup>50</sup> We must also look to other countries for novel and innovative schemes to reduce the cost of medicines, especially with projected increases in healthcare costs in the future, and look how these may work on a holistic level – for the patient and in the national context. Laterally, this review also highlights the potential role of the pharmacy profession in medicines access; deregulation is one example, in some European countries this has increased access of medicines to the public, by increasing the number of pharmacies that have been established.

Whilst this review highlights many themes for consideration to potential policy decision-makers, there are several limitations. Firstly, bias in terms of publication and outcome reporting bias may have led to publication or non-publication of articles depending on the

nature or direction of the finding of which we cannot account for.<sup>9</sup> We also need to bear in mind bias could be included from articles that had associations with organisations, i.e. that were written by consultants to the industry. Articles were only included if an English language version was available; if a publication was in another language alone, it was excluded. With consideration of these limitations, our review provides important insights into pharmaceutical policy in Australia and New Zealand and its impact upon patient access to medicines in each country.

## Conclusion

A variety of pharmaceutical policies have been reported in this review, which illustrate the similarities and differences between Australia and New Zealand, in reference to policies that affect medicines access. Key differences between the two countries include differences in marketing authorization and medicines registration policies with Australia implementing parallel processing policies to enhance the time from regulatory submission to subsidised access in the country. Australia appears to cover and reimburse a greater number of medicines while New Zealand achieves much lower prices for medicines than their Australian counterparts and has been more successful in controlling national pharmaceutical expenditure. Delays in patient access to new therapies in New Zealand have considerable implications for overall patient access to medicines, however, higher patient co-payments and relative pharmaceutical expenditure in Australia and its effect upon patient access to medicines must also be considered.

**726 Author Contributions**

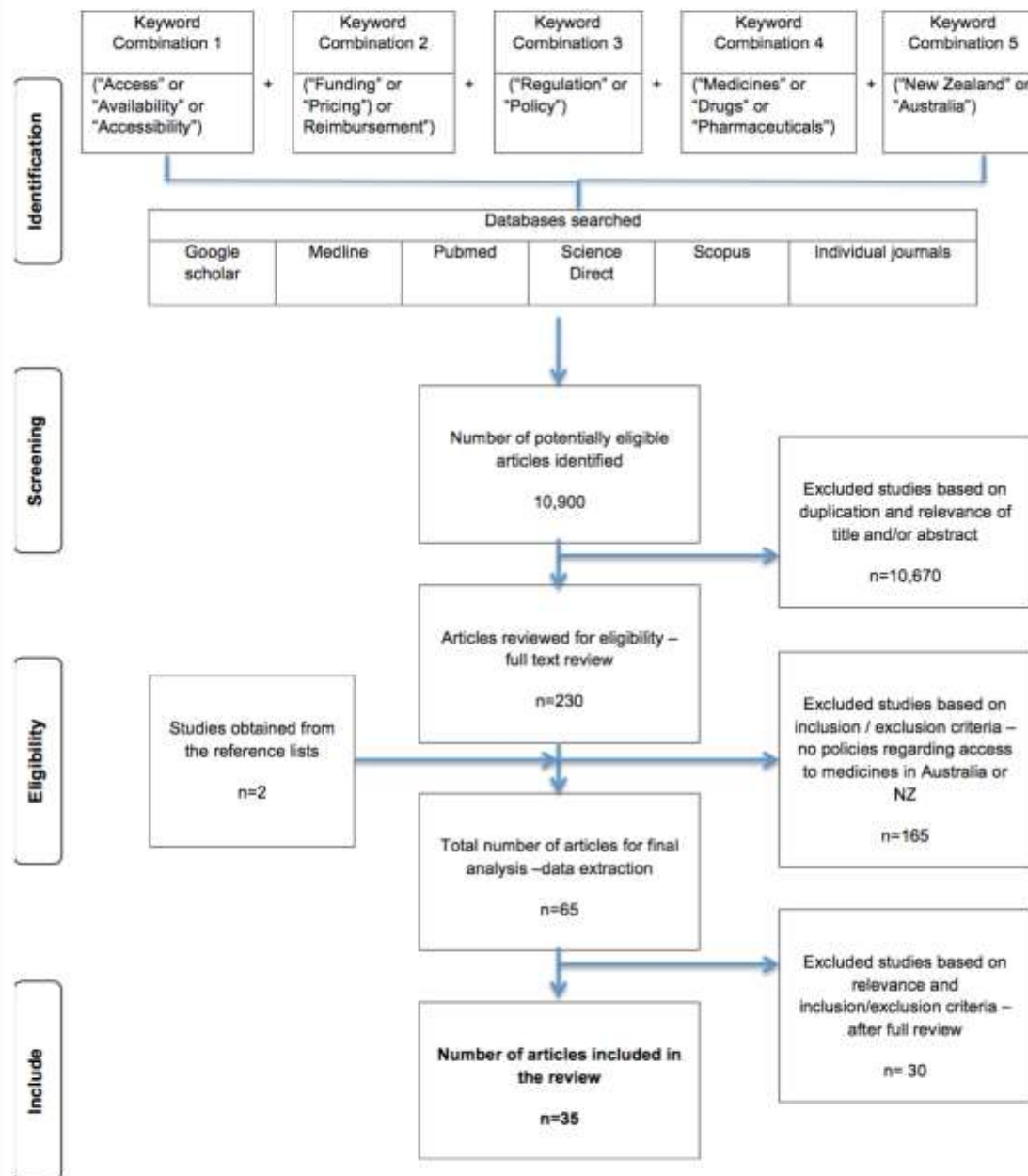
727 Conceived and designed the experiments: ZB, TG. Performed the experiments: TG, AS.

728 Analyzed the data: TG AS, ZB, revised by LC.

729 Contributed reagents/materials/analysis tools: TG AS, ZB, revised by LC.

730 Wrote the paper: TG, AS, ZB, significantly revised by LC

Figure 1: Process of identification, screening, eligibility and inclusion in this systematic review



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733 **Table 1.** Study inclusion & exclusion criteria.

<i>No</i>	<i>Category</i>	<i>Inclusion Criteria</i>
1	Year of release	2008-2016
2	Publication Type	Full text articles in peer-reviewed scientific journals and in English
3	Countries Covered	Australia and New Zealand
4	Kinds of Medicines	Brand name drugs
5	Definition and issues to include	<p>Medicines, access, (specialised) clinicians, biologicals, (patient) access, policy &amp; regulation.</p> <ul style="list-style-type: none"> <li>• Definitions of pharmaceuticals / medicines</li> <li>• (Patient) access, drug availability or accessibility</li> <li>• Marketing authorization, approval processes</li> <li>• Legislation, policy, regulation</li> <li>• Licensing, pricing, funding, health technology assessment, reimbursement</li> <li>• Other relevant legislation/access factors</li> </ul>
6	Methodology and topic of research	Review of peer reviewed journal articles investigating political and regulatory mechanisms in Australia and New Zealand by which medicines are accessed, funded and reimbursed and the mechanisms that define these aspects of pharmaceutical policy and medicine access.
7	Outcomes of regulation or policy	Pharmaceutical policies in New Zealand and Australia that facilitate or hinder (patient) access, funding and reimbursement of medicines in either country.
8.	Bias	<p>No presence of issues in study design, methods, data collection, analysis or any other factor of the study or article that could lead to bias of the individual study.</p> <p><i>Exclusion Criteria</i></p>
1		Articles that are not published in the English Language
2		News Reports

734 Table 2 Themes and sub-themes extracted from the included literature.

Themes	Sub-Themes
National Health System	<ul style="list-style-type: none"> <li>• National Health Policy</li> <li>• Pharmacy System</li> <li>• Marketing Authorization and Regulation</li> <li>• Prescription to Non-Prescription Medicine Switch</li> <li>• Orphan Drug Policies</li> </ul>
Pricing	<ul style="list-style-type: none"> <li>• Generic Medicine Substitution</li> </ul>
Reimbursement	<ul style="list-style-type: none"> <li>• National Pharmaceutical Schedule &amp; Health Technology Assessment</li> <li>• Patient Co-Payments</li> <li>• Managed Entry Agreements</li> </ul>

**Table 3:** An overview of pharmaceutical policies influencing access to medicines and their implementation in Australia and New Zealand.

Country Covered	National Health Policy – Overview (Reference)	Pharmacy System (Ref)	Marketing Authorization and Regulation – Overview and Timing, Parallel Processing (Y/N) (Ref)	Prescription to Non Prescription Medicine Switch (Ref)	Orphan Drug Policies (Ref)	Pricing (Ref)	Generic Medicine Substitution – Policies and Incentives (Ref)	Patient Co-payments- Extent and Policies(Ref)	Reimbursement 1. Procedures and/or coverage 2. HTA Criteria
<b>Australia (AUS)</b>	<p>National Public Health System with a mix of public and private funding</p> <p>The national (commonwealth) government funds two thirds of total healthcare spending while the other third is funded by other, lower levels of national and state government.</p> <p>Patient out of pocket expenditure accounts for 17% of total expenditure on health care</p> <p>National Medicines Policy provides the framework for the regulation and funding of medicines in AUS.</p> <p>(4 ,5, 12)</p>	<p>Over 6, 663 pharmacies and chemists distributed across AUS.</p> <p>Pharmacies and their ownership are governed by state and federal legislation.</p> <p>Pharmacy ownership restricted (in large part) to registered pharmacists</p> <p>Majority owned by pharmacists with a small number owned by non-profit entities.</p> <p>Pharmacies also provide a range of other, usually primary health care services including preventative care and medication management. (12, 15)</p>	<p>Applications for registration and marketing of new medicines conducted by the Australian Therapeutic Goods Administration (TGA).</p> <p>Submission to the TGA for medicine registration can be conducted alongside submission to the pharmaceutical Benefits Advisory Committee (PBAC) who operate the pharmaceutical benefits scheme (PBS) in AUS.</p> <p>Standard registration process takes 52 weeks (12 months)</p> <p>Minimum time from regulatory submission to subsidised access = 72 weeks (Y)</p> <p>(3, 5 ,12, 15)</p>	<p>AUS has four categories of medicines; prescription, general sales, pharmacy only, and pharmacist only.</p> <p>AUS does not have an overall governmental position on medicine switch.</p> <p>The Secretary to the Department of Health or their respective delegates makes the final decision on switch.</p> <p>(6, 19)</p>	<p>Yes – Australia's national orphan drug policy and under consideration within Australia's life-saving drug's programme</p> <p>(10, 11)</p>	<p>Fixed - Reference and value based pricing</p> <p>No governmental price regulation of medicines not on the national schedule</p> <p>(10, 12, 20-22)</p>	<p>Brand Premium Policy- Reference pricing system where the government subsidises only up to the price of the lowest price brand</p> <p>Generic Substitution Policy- Allows community pharmacists to voluntarily substitute specified PBS-listed named medicines with the equivalent generic medicine</p> <p>(12, 24- 26)</p>	<p>General patient co-payments are AU \$37.70 (US \$29.39)</p> <p>Concession card holders AU \$6.10 (US \$ 4.76)</p> <p>Safety Net Thresholds of AU \$1421.20 for general patients and AU \$360 for concessional patients – Once threshold is reached, patients receive all remaining prescriptions free for that (financial) year</p> <p>(5, 11, 12, 25)</p>	<p>1. The subsidisation of medicines is managed by the AUS department of health with advice provided by the Pharmaceutical Benefits Advisory Committee (PBAC). This combination lists new medicines and indications on the pharmaceutical benefits schedule (PBS) which is the national pharmaceutical schedule of subsidised medicines for the country. PBAC does not operate under a capped budget however any medicine expected to exceed AU \$20 million per year must be approved by Cabinet.</p> <p>2. PBAC considers efficacy, safety, cost-effectiveness and budget impact. Overall this makes up a proportion of a capped health budget.</p> <p>Economic analysis methods utilised included cost utility/ effectiveness analysis and cost minimisation analysis (CUA/CEA and CMA)</p> <p>(4, 5, 12, 15, 27)</p>

Country Covered	National Health Policy – Overview (Reference)	Pharmacy System (Ref)	Marketing Authorization and Regulation – Overview and Timing, Parallel Processing (Y/N) (Ref)	Prescription to Non Prescription Medicine Switch (Ref)	Orphan Drug Policies (Ref)	Pricing (Ref)	Generic Medicine Substitution – Policies and Incentives (Ref)	Patient Co-payments- Extent and Policies(Ref)	Reimbursement 1. Procedures and/or coverage 2. HTA Criteria
<b>New Zealand (NZL)</b>	<p>National Public Health System with a mix of public and private funding</p> <p>80% of NZL expenditure on health care is publically funded.</p> <p>20 District Health Boards across NZL are responsible for public health services for their respective populations</p> <p>(4, 5, 13)</p>	<p>Approximately 1000 pharmacies distributed across New Zealand.</p> <p>Pharmacies must hold a license under the Medicines Act 1981 that allows operation if a NZL registered pharmacist is present,</p> <p>Pharmacies may be owner by a sole individual, partnership or company however the majority share must be held by a single or group of NZL registered pharmacists.</p> <p>Pharmacies are also involved in primary health care services under contract of DHBs.</p> <p>(13)</p>	<p>The New Zealand Medicines and Medical Devices Safety Authority (Medsafe) is responsible for applications for registration and marketing of new medicines in NZL.</p> <p>Positive recommendation by Medsafe is required before submission to PHARMAC for a decision on inclusion on the national pharmaceutical schedule.</p> <p>Standard registration process takes 52 weeks (12 months)</p> <p>Minimum time from regulatory submission to subsidised access = 84 weeks</p> <p>(N)</p> <p>(3, 5, 13)</p>	<p>NZL has four categories of medicines; prescription, general sales, pharmacy only, and pharmacist only.</p> <p>The Medicines Classification Committee (MCC), operates a Ministerial advisory committee, recommends classifications of medicines to one of the four categories of medicine and is operated by Medsafe in NZL.</p> <p>(6, 19)</p>	<p>No overall policy</p> <p>PHARMAC do possess a \$5 million orphan drugs fund for inclusion of orphan medicines on the national pharmaceutical schedule</p> <p>(10, 11)</p>	<p>Fixed - Reference Pricing, competitive tendering, price negotiations for medicines on the national reimbursement schedule</p> <p>No governmental price regulation of medicines not on the national schedule</p> <p>(13, 23)</p>	<p>Competitive tendering between generic manufacturers based upon reference pricing</p> <p>Switch to generic medicines as medicines come off patent (re-tendering)</p> <p>(13)</p>	<p>NZ\$ 5 (US \$3.76) for all patients besides Children under 13 years which receive subsidised medicines free of charge.</p> <p>(5, 13, 20)</p>	<p>1. The New Zealand Pharmaceutical Management Agency (PHARMAC) operates the national pharmaceutical schedule for subsidised medicines and lists new medicines, indications and medical devices on the national schedule. PHARMAC administers the schedule alone and the NZL government or judiciary cannot block any listing.</p> <p>PHARMAC operates within a defined funding envelope which allows a fixed budget for listing of new medicines each year.</p> <p>2. PHARMAC currently considers nine 'decision' criteria upon which funding decision are made, these criteria include cost-effectiveness, budget impact, efficacy, safety and other relevant political factors.</p> <p>PHARMAC primarily utilise cost-utility analysis (CUA) in economic analyses.</p> <p>(4, 5, 13, 20, 28)</p>

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886 **Supporting Information**

887 **Appendix One: PRISMA Checklist**

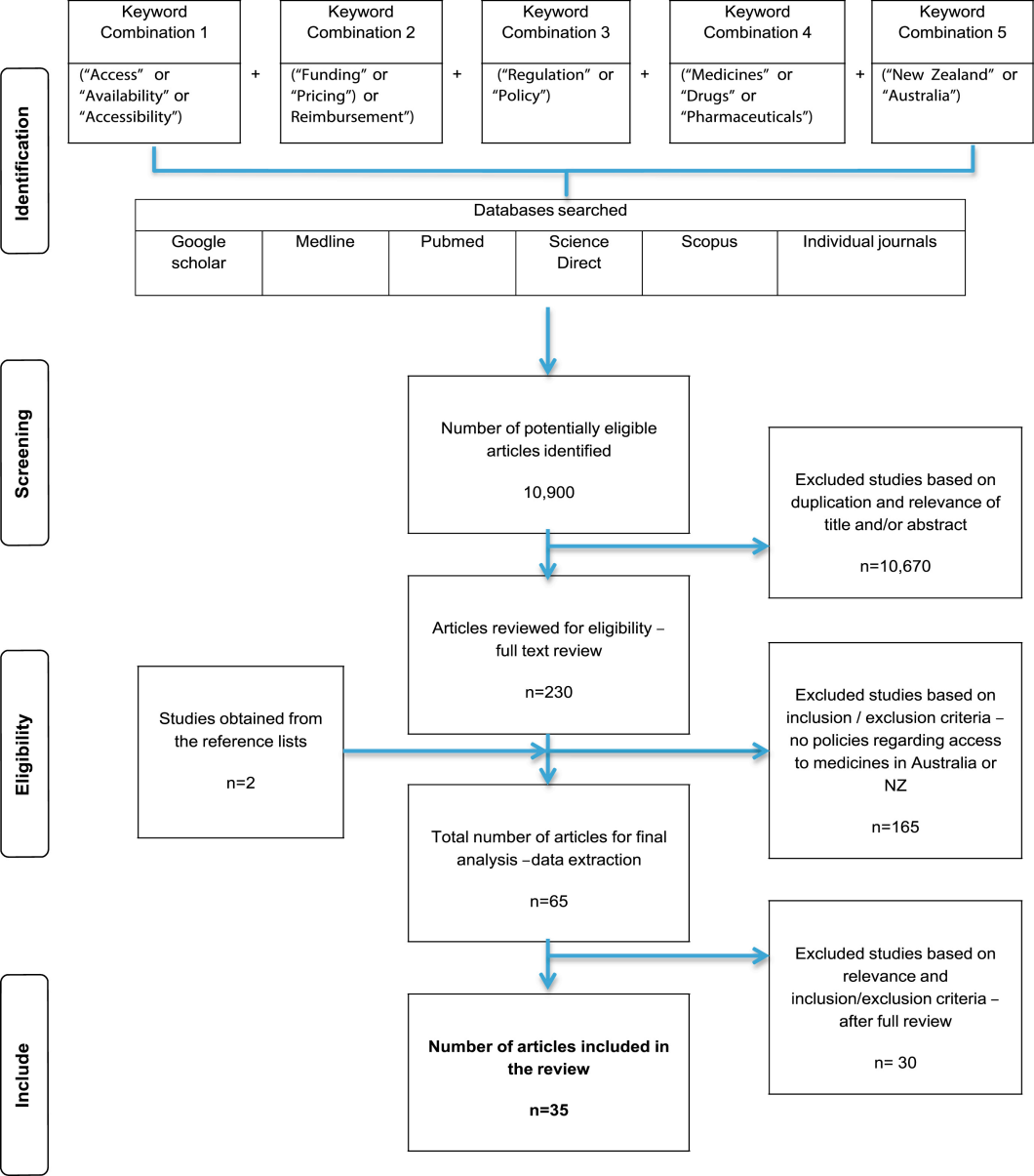
888 **Appendix Two: General Characteristics of Included Studies**

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## Highlights

- This review has identified key areas of difference in medicines policy between Australia and NZ which potentially could influence patient access to medicines; and drug prices and reimbursement status in each country
- Australia and New Zealand differed in terms of marketing authorization and regulation with parallel processing available in Australia, enhanced medicine switch in New Zealand and a lack of orphan drug legislation in New Zealand.
- New Zealand achieved much lower prices for medicines and required lower patient co-payments and has been more successful in controlling national pharmaceutical expenditure while Australia appeared to fund a greater number of medicines on their national pharmaceutical schedule.
- Delays in patient access to new therapies in New Zealand have considerable implications for overall patient access to medicines, however, higher patient co-payments and relative pharmaceutical expenditure in Australia and its effect upon patient access to medicines must also be considered.
- This critical analysis allows for the evaluation of policies that affect patient access to medicines and thus could potentially better inform policy decision-makers moving forward when considering access to medicines.